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Multimodal Therapy for Neoplasms Arising From a Vesical Diverticulum

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Both radical cystectomy and diverticulectomy for the treatment of neoplasms arising in a vesical diverticulum have resulted in poor survival, mainly secondary to early metastatic spread. In this study, nine patients were treated with a multispecialty approach in hopes of eradicating both local and distant disease. All patients underwent a combination of therapeutic modalities with three patients undergoing pre-operative radiotherapy (RT) and diverticulectomy; diverticulectomy and chemotherapy (three patients); diverticulectomy with chemotherapy and pre-operative RT (two patients); and definitive RT with cisplatin (one patient). With a mean follow-up of 4.0 years (median 3.2), four patients are free of disease, two are dead of other causes, one patient has developed an invasive recurrence, one patient is alive with metastatic disease, and one patient is dead of disease. Five patients (55%) developed local recurrences. Disease-specific survival for the group was 89%. Surgical monotherapy has been ineffective in controlling both local and metastatic disease in patients with diverticular tumors. This study suggests a significant benefit from systemic chemotherapy and RT when combined with surgery for these neoplasms.

KEY WORDS: **bladder diverticulum, radiotherapy, chemotherapy, carcinoma**

INTRODUCTION

The incidence of neoplasms from a vesical diverticulum has been reported at 2–13% [1–5]. These lesions tend to carry a poor prognosis due mainly to early dissemination of disease [2–4]. It is felt that lack of a muscular layer overlying the diverticulum contributes to the early spread of metastases [1]. In the few reported series of diverticular tumors, either radical cystectomy or vesical diverticulectomy were utilized despite the near uniformly poor survival rates with surgery alone [2–4]. Generally, both disease-free and 5-year survival are felt to be $<10\%$ [6].

In an effort to improve on the results achieved with surgical monotherapy, a multispecialty approach using radiation therapy (RT), chemotherapy and surgery, was applied. We report the first series in which systemic chemotherapy and RT were routinely utilized in the treatment of vesical diverticular tumors.

MATERIALS AND METHODS

From 1982 to 1993, nine patients were treated for neoplasms arising from a vesical diverticulum. All patients were male in the age range of 51–72, and no patient had a previous history of bladder cancer. Seven patients presented with hematuria, whereas two presented with obstructive symptoms. The diagnosis was made by either cold cup biopsy or transurethral debulking. Complete tumor resection was not attempted due to the increased risk of tumor spillage; therefore, initial clinical stage was not available. Negative random biopsies including the prostatic urethra were obtained in all patients. All nine patients were noted to have transitional cell carcinoma, of which seven were grade 3/3 lesions and two were grade 2/3 lesions. In addition, patients underwent routine staging with intravenous pyelogram, abdominal CT scan, chest X-ray, and liver function studies. Each patient then received a combination of at least two therapeutic modalities; no patient was treated with surgical monotherapy

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TABLE I. Treatment of Patients With Neoplasms Arising in a Vesical Diverticulum

	No. of patients
Diverticulectomy and pre-operative radiotherapy	3
Diverticulectomy and chemotherapy	3
Diverticulectomy, pre-operative radiotherapy and chemotherapy	2
Radiotherapy (65 Gy) and cisplatin	1
Total	9

TABLE II. Recurrences in Patients With Diverticular Neoplasms

Pt.	Stage	Grade	Treatment[a]	Outcome[b]	Residual tumor
1	TA	2	TUR, IVC	Alive	No
2	metastases	3	resection	Alive	Yes
3	metastases	3	none	DOD	Yes
4	T1	3	TUR, IVC	DOC	No
5	TA	1	TUR	DOC	No
6	T2	3	TUR, IVC	Alive	Yes

[a]TUR = transurethral resection; IVC = intravesical chemotherapy.
[b]DOD = dead of disease; DOC = dead of other cause.

(Table I). Vesical diverticulectomy with ipsilateral pelvic lymphadenectomy was done in eight patients. Pre-operative RT (45 Gy) was administered to five patients. One patient refused diverticulectomy and therefore was treated with full dose RT (65 Gy) in combination with three cycles of cisplatin. Neo-adjuvant chemotherapy was administered to three patients in the form of MCV (methotrexate, cisplatin, and vinblastine) to two patients and MVAC (methotrexate, vinblastine, adriamycin, and cisplatin) to one patient. Adjuvant chemotherapy was also administered in the form of MCV to two patients and MVAC to one patient.

RESULTS

Pathologic examination from the eight patients undergoing vesical diverticulectomy revealed no evidence of disease (P0) in five patients, carcinoma in situ (CIS) in one patient, and invasive disease (T3b) in two patients. At a mean follow-up of 4.0 years (median 3.2), four patients are alive without evidence of disease; two patients are dead of other causes without disease at 37 and 48 months. One patient is alive at 47 months, status-post resection of a solitary metastasis, and one patient is dead of disease at 17 months (Table II). The patient who initially refused diverticulectomy is alive at 9.6 years with locally invasive disease. Disease-specific survival for the group was 89% (Table III).

There have been 15 local recurrences in five patients (55%). All recurrences were treated with transurethral resection with the addition of intravesical chemotherapy when indicated. The only invasive recurrence occurred in the patient who refused the diverticulectomy.

DISCUSSION

The incidence of neoplasms arising from a vesical diverticulum has been reported at 2–13% [1–5], although histologic changes have been noted in up to 84% of diverticula excised for benign disease [2,7]. Urinary stasis within the diverticulum is felt to be an important factor in the carcinogenesis of these lesions. These carcinomas are frequently associated with early dissemination of metastatic disease and usually portend to a poor prognosis.

There have been previous reports of clinically localized diverticular carcinomas in which either radical cystectomy or diverticulectomy was utilized as the mainstay of therapy [2–5]. Kelalis and McLean [2] described 19 patients with diverticular neoplasms treated with primarily surgical excision in which they noted a cancer-specific survival of 16% at 2 years. Faysal and Freiha described 12 patients also treated with primarily surgical excision. They reported a cancer-specific survival of 25%, and a disease-free survival of 8% with an average follow-up of 2.3 years [3]. Similarly, Micic et al. [4] reported 13 patients treated with surgical excision and noted a cancer-specific survival of 46%. Conversely, Montague and Boltuch [5] reported improved survival in a series of 10 patients with predominately surgical excision. They felt that early diagnosis and treatment was the reason for improved survival in their group.

In view of the poor results with surgical monotherapy, our group was treated using a multidisciplinary approach. Disease-specific survival in this study was 89% with a mean follow-up of 4 years. Of the eight patients who underwent diverticulectomy, none ultimately required radical cystectomy; however, an invasive recurrence did develop in the patient who had refused diverticulectomy. Of the two patients who developed metastatic disease, only one local recurrence developed (CIS), suggesting that diverticulectomy offers adequate control of local disease in these cases.

Pre-operative RT was administered to five patients in our group. Although not widely used for patients with bladder cancer, pre-operative RT may be beneficial to patients undergoing diverticulectomy or partial cystectomy. Van der Werf-Messing has shown a decrease in the incidence of both local recurrence and wound implantation in patients with invasive bladder cancer treated with pre-operative RT [8].

As these tumors frequently metastasize early in their course, it appears rational to offer systemic therapy for what is commonly a systemic disease. Five patients in this study were treated with neo-adjuvant and/or adjuvant chemotherapy in an effort to eradicate micro-metastatic disease. Although there have been no definitive studies supporting the use of neo-adjuvant chemotherapy, two recent studies have demonstrated a clear advantage to the

TABLE III. Survival in Patients With Diverticular Neoplasms

Patient	Initial grade	Initial treatment[a]	Pathologic stage	Alive (mos.)	Dead (mos.)	Residual tumor
1	2	neo, surg	P0	70		No
2	3	neo, surg	P0	47		Yes
3	3	RT, surg, adj	T3b		18	Yes
4	3	RT, surg	P0		48	No
5	3	RT, surg, adj	T3b		37	No
6	3	RT, cisplatin	—	115		Yes
7	3	RT, surg	P0	35		No
8	3	neo, surg, adj	P0	24		No
9	2	RT, surg	CIS[b]	38		No

[a]neo = neo-adjuvant chemotherapy, surg = surgery, RT = radiotherapy, adj = adjuvant chemotherapy,
[b]CIS = carcinoma in situ;
— = patient refused surgery.

use of adjuvant chemotherapy for patients with locally advanced bladder cancer [9,10].

Currently, for patients with diverticular neoplasms who are appropriate candidates, we offer pre-operative RT followed by vesical diverticulectomy. We then recommend three cycles of cisplatin-based chemotherapy in order to eradicate residual metastatic disease.

CONCLUSIONS

Due to the poor survival with surgery alone, improved forms of therapy are needed for patients with vesical diverticular neoplasms. Our study suggests that the addition of systemic chemotherapy and pre-operative RT may improve on the results of surgery alone.

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